JNJ-39758979

Cat. No.: HY-101189

CAS No.: 1046447-90-8

Molecular Formula: $C_{11}H_{19}N_5$

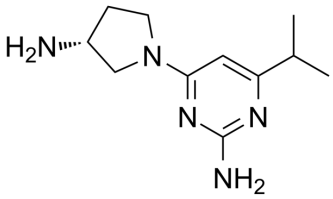
Molecular Weight: 221.3

Target: Histamine Receptor

Pathway: GPCR/G Protein; Immunology/Inflammation; Neuronal Signaling

Storage: 4°C, protect from light

* In solvent : -80°C, 6 months; -20°C, 1 month (protect from light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 33.33 mg/mL (150.61 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	4.5188 mL	22.5938 mL	45.1875 mL
	5 mM	0.9038 mL	4.5188 mL	9.0375 mL
	10 mM	0.4519 mL	2.2594 mL	4.5188 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 3.5 mg/mL (15.82 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 3.5 mg/mL (15.82 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 3.5 mg/mL (15.82 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

JNJ-39758979 is a selective, orally active, and high-affinity histamine H_4 receptor antagonist with K_is of 12.5, 5.3, and 25 nM for human, mouse, and monkey histamine H_4 receptor, respectively. JNJ-39758979 functionally antagonizes histamine-induced cAMP inhibition with a pA2 of 7.9 in transfected cells. JNJ-39758979 shows good anti-inflammatory and antipruritic activity[1][2].

IC_{50} & Target

Human H_4 Receptor	Mouse H_4 Receptor	Monkey H_4 receptor	Rat H_4 receptor
12.5 nM (Ki)	5.3 nM (Ki)	25 nM (Ki)	188 nM (Ki)

Guinea pig H_4 receptor

	306 nM (Ki)
In Vitro	JNJ 39758979 is a selective, high-affinity histamine H_4 receptor antagonist with a K_i of 12.5 nM versus the human H_4 receptor and functionally antagonizes histamine-induced cAMP inhibition with a pA2 of 7.9 in transfected cells. At the mouse H_4R, the K_i=5.3 nM and the pA2=8.3. At the monkey H_4R, the K_i=25 nM and the pA2=7.5. The affinity for the rat (K_i=188 nM, pA2 = 7.2) and guinea pig H_4R (K_i=306 nM) is moderate, and JNJ 39758979 has little if any affinity for the dog H_4R (K_i≥10 μM). The compound is highly selective for H_4R, as it exhibits low affinity for the H_1, H_2, and H_3 receptors[1]. JNJ-39758979 is metabolically stable ($t_{1/2}$ >120 min) when incubated in vitro with human, rat, dog, or monkey liver microsomes[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	JNJ-39758979 (10 mg/kg; p.o.) treatment shows that the C_{max}, $t_{1/2}$ and F values are 0.3 μM, 7.5 hours, and 36%, respectively [1]. JNJ-39758979 (2 mg/kg; i.v.) treatment shows that the Vss, AUC, CL and $t_{1/2}$ were 19.9 L/kg, 1.4 μM*h, 2.2 L/h, and 2.1 hours, respectively [1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Sprague-Dawley rats[1]
Dosage:	10 mg/kg
Administration:	Oral administration (Pharmacokinetic Analysis)
Result:	The C_{max}, $t_{1/2}$ and F values were 0.3 μM, 7.5 hours, and 36%, respectively.

REFERENCES

[1]. Savall BM, et al. Discovery and SAR of 6-alkyl-2,4-diaminopyrimidines as histamine H4 receptor antagonists. J Med Chem. 2014 Mar 27;57(6):2429-39.

[2]. Murata Y, et al. Phase 2a, randomized, double-blind, placebo-controlled, multicenter, parallel-group study of a H4 R-antagonist (JNJ-39758979) in Japanese adults with moderate atopic dermatitis.

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